

multiplexed bead-based assays. Optionally, the beads may have a size sufficient to define a suspension within the surrounding test fluid. In some embodiments, the beads may comprise a colloid within the test fluid. In some embodiments, beads 64 may be movably supported by a surface of a vessel containing the test fluid, for example, being disposed on the bottom surface of the vessel (where beads 64 have a density greater than that of the test fluid). In other embodiments, the beads may be affixed to a support structure and/or to each other. Still further alternatives are possible, such as for beads 64 to be floating on an upper surface of the test fluid, for the bead or beads to be affixed to or disposed between cooperating surfaces of the vessel to maintain the positioning of the bead or beads, for the bead or beads to be disposed at the interface between two fluids, and the like.

Please replace the last paragraph started on page 29 with the following (so as to replace "bead 64" with "bead 64x", "bead 64" with "bead 64y" and "individual bead 64" with --individual bead 64x-- respectively):

As was described above, it will often be advantageous to include numerous beads 64 within a single test fluid so as to perform a plurality of assays. Similarly, it will often be advantageous to identify a large number of fluids or small discreet elements within a single viewing area without separating out each spectral label from the combined labeled elements. As illustrated in Fig. 4, the dispersed spectral image 68 of bead 64x upon sensor 56 will depend on both the relative spectra generated by the bead, and on the position of the bead. For example, bead 64y is imaged onto a different portion 68' of sensor 56, which could lead to misinterpretation of the wavelengths of the spectra if the location of bead 64y is not known. So long as an individual bead 64x can be accurately aligned with the imaging optics 58 and sensor system 66, absolute spectral information can be obtained. However, as can be understood with reference to Fig. 5A, a plurality of beads 64 will often be distributed throughout an area 70.

Please replace the first full paragraph on page 30 with the following (so as to replace "slit viewing field 74" with --slit view of sensing field 74--):

To ensure that only beads 64 which are aligned along an optical axis 72 are imaged onto sensor 56, aperture 62 restricts a sensing field 74 of the sensing system. Where sensor 56 comprises an areal sensor such a charge couple device (CCD), aperture 62 may

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cont

comprise a slit aperture so that spectral wavelengths λ can be determined from the position of the dispersed images 68 along a dispersion axis of wavelength dispersive element 54 for multiple beads 64 distributed along the slit view of sensing field 74 along a second axis y , as can be understood with reference to Fig. 5B. Absolute accuracy of the spectral readings will vary inversely with a width of aperture slit 62, and the number of readings (and hence total reading time) for reading all the beads in area 70 will be longer as the slit gets narrower. Nonetheless, the beads 64 within the two-dimensional area 70 may eventually be read by the system of Figs. 5A and 5B with a scanning system which moves the slit relative to beads 64 (using any of a variety of scanning mechanisms, such as movable mirrors, a movable aperture, a flow of the beads passed a fixed aperture, a movement of the surface of the vessel relative to the aperture, or the like).

Please replace the first paragraph on page 33 with the following (so as to add the reference number --96-- after "spectrally dispersed images" at the end of line 10):

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Correlation of the positioning image 88 with the spectrally dispersed image 68 can be understood with Figs. 6A through 6C. Positioning image 88 generally indicates positions of beads 64 within sensing field 81, while spectrally dispersed image 68 reflects both the position and spectral wavelengths of each signal within the spectra generated by beads 64. Using an accurately calibrated system, analyzer 90 can determine the absolute wavelengths of a particular dispersed image 96a by identifying the associated bead position 64a, particularly where beads 64 do not overlap along the y -axis. As can be understood with reference to Figs. 6B and 6C, correlation of beads' locations and spectrally dispersed images 96 may be facilitated by including a calibration signal 40c within at least one of the spectra generated by a bead. Such calibration signals will often be included in at least some of the bead spectra, optionally being included in each bead spectrum. Where the calibration signal wavelength is known, the location of the associated bead along the x -axis can be determined from the location of the calibration signal energy within the dispersed image 68 from the diffracting characteristics of wavelength dispersive element 54.

Please replace the third full paragraph on page 37 with the following (so as to add the reference number --122-- after "image the sensing field upon a surface" on line 17):

ay To allow scanning/imaging system 120 to detect relatively low-intensity signals within the two-dimensional sensing field 81, optics 58 image the sensing field upon a surface 122 of sensor 56. A spectral filter 128 selectively transmits marker signals 102 to sensor 56 of the detector, thereby avoiding saturation from the relatively high-intensity spectral label signals. Using our simple marker/label separation scheme illustrated in Fig. 8, filter 128 may comprise a dichroic filter which selectively transmits the marker signals within second range 112b. Clearly, more complex filtering and signal separation arrangements are possible. Regardless, as numerous beads 64 within two-dimensional sensing field 81 can have their assay markers detected simultaneously, a relatively long integration time may be employed without adding excessively to the overall sensing time.

Please insert the following new paragraph before the heading Fabrication of Labeled Beads on page 19 of the specification as follows.

as --An exemplary processor is illustrated in FIG. 1A. A processor includes data input devices, a serial port connector, an interface card, a USB Connector, a parallel port connector, an input device, a printer for hard copies, a CPU, a monitor to view data, an internal memory to store data, long term storage (Floppy, CD, Hard Disk, Cartridge, Other), image processing software, data analysis software (decodes spectra and assay signals), data processing software and database.--

IN THE CLAIMS:

All pending claims have been reproduced below for the Examiner's convenience. Please amend claims 1, 3, 12, and 17; please cancel claims 2 and 20-57; and please add new claim 58.

- as
- 1 58
 - 2 31
 - 3
1. (Amended) A system comprising:
a plurality of labels generating identifiable spectra in response to excitation energy, wherein at least some of the spectra comprise a plurality of signals for each label, the